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Ethanol-Induced Apoptosis of Interneurons in the Neonatal GAD67-GFP Mouse Hippocampus

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Abstract

© 2016, Springer Science+Business Media New York.Ethanol induces massive neuroapoptosis in the developing brain. However, whether ethanol-induced neuroapoptosis also involves GABA interneurons remains unknown. Here, we addressed this question in the postnatal days (P) P3-P24 GAD67-GFP mouse hippocampus using cleaved caspase-3 staining, a sensitive measure of ethanol-induced apoptotic neurodegeneration combined with DAPI staining to monitor the apoptotic nuclear degradation. We observed that 8 h following ethanol treatment (6 g/kg, intraperiotoneally), significant proportion of GAD67-GFP expressing hippocampal interneurons was stained with cleaved caspase-3 antibodies and displayed chromatin condensation with a formation of the DAPI-stained apoptotic bodies. Maximal number of the cleaved caspase-3 stained interneurons (16.6 % of the total number of GFP expressing neurons and 21.6 % of the total number of caspase-3 stained cells) was observed in the hippocampal slices from P6-9 mice, and minimal damage to interneurons was observed in P3–4 and > P11 mice. While the apoptotic interneurons were found in all hippocampal regions and layers, their highest density was observed in the CA1 region and hilus. Thus, ethanol-induced neuroapoptosis involves hippocampal interneurons that may contribute to the life-long neurobehavioral deficits, increased excitability, and higher incidence of seizures characteristic of the fetal alcohol spectrum disorders.

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Keywords

Alcoholism, Fetal alcohol syndrome, GABA, Hippocampus, Interneurons, Neonate

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